Reg. Std. File

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 27 1992

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Asulam-Sodium Salt Technical Reregistration: Rhone-Poulenc Response to Asulam-sodium salt (Case No. 0265, Chemical No. 106902) Reregistration Product Chemistry Data Requirements Regarding Physical Chemical Characteristics [Odor, Melting Point, Solubility, Dissociation Constant, Storage Stability, & Corrosion Characteristics (Guideline # 63-4, 63-5, 63-8, 63-10, 63-17, & 63-20).
(MRID No. 42342001, 42342002, 42342003, & 42342004)
CBRS # 10086; DP BARCODE: D179485).

FROM: Freshteh Toghrol, Ph.D., Chemist F. Toghrol
Reregistration Section II
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Health Effects Division (H7509C)

THRU: William J. Hazel, Ph.D., Section Head W. J. Hazel
Reregistration Section II
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TO: Linda Propst/C. Peterson, PM Team 73
Reregistration Branch
Special Review and Reregistration Division (H7508W)

Rhone-Poulenc AG Company has responded to the asulam-sodium salt (methylsulfanilylcarbamate, sodium salt) reregistration product chemistry data requirement regarding odor, melting point, solubility, & dissociation constant (Guideline # 63-4, 63-5, 63-8, & 63-10).

The registrant has also requested data waivers for asulam-sodium salt product chemistry regarding storage stability and corrosion characteristics (Guideline # 63-17 and 63-20), reasoning that this product is a TGAI and not an MP.

CBRS General Conclusions Regarding Odor (63-4), Melting point (63-5), Solubility (63-8) and Dissociation Constant (63-10) of Asulam:

These product chemistry deficiencies odor (63-4), melting point (63-5), solubility (63-8) and dissociation constant (63-10) for asulam sodium salt technical of Rhone-Poulenc AG Company are resolved.

CBRS presently recommends against the data waivers for asulam-sodium salt regarding storage stability and corrosion characteristics (Guideline # 63-17 and 63-20) because it is not clear to us whether asulam-sodium salt is an unregistered TGAI (that will be used to support the registration of end-use products) or if it is an MP as well as a TGAI (see our note to PMs in this memo).

Detailed Consideration:

We will restate the data requirements for Rhone-Poulenc's asulam sodium salt (TGAI) product chemistry below regarding odor, melting point, solubility, and dissociation constant followed by the registrant's response and our comments.

Data Requirement: Regarding Odor (Guideline # 63-4)

Asulam Product and Residue Chemistry Reregistration Standard Update (dated 1/15/91) indicated that Rhone-Poulenc has responded to data requirement for the 86.4% T (MRID 40751501); however, a more qualitative description of the odor is required.

Registrant's Response to Data Requirement: Regarding Odor (Guideline # 63-4)

The registrant has provided data (MRID 42342001) on the odor of asulam-sodium salt with 90.7% purity (batch No. EN 50005). 3 gram asulam-sodium technical grade was transferred into a glass container and equilibrated in a thermostated water bath at 25 °C for 24 hours. The sample was removed from the water bath and no odor was detected. It was concluded that asulam-sodium salt technical is odorless.

CBRS Comment Regarding Data provided for Odor:

This deficiency is resolved for the asulam-sodium salt TGAI.

Data Requirement: Regarding Melting Point (Guideline # 63-5)

Asulam Product and Residue Chemistry Reregistration Standard Update (dated 1/15/91) indicated that Rhone-Poulenc has responded to data requirements for the 86.4% T (MRID 40751501; EPA Reg. No. 264-451); however, an actual melting point value is required.

Registrant's Response to Data Requirement: Regarding Melting Point (Guideline # 63-5)

The registrant has provided data (MRID 42342002) on the melting point of asulam-sodium salt TGAI with 88.4% and 89.4% purity (batch No. 36112 and 36085, respectively). The melting point was determined using two different calorimetric methods: a duPont 990 Thermal Analyzer which was equipped with a DSC 910 cell Base Module and a DSC cell with a Boersma type measuring head. Another melting point determination was carried out using a visualized capillary melting point instrument Buchi 510. Melting point tests indicated 212, 212, 214, and 215 °C using the first method and 214 °C with the second method. It was concluded that asulam-sodium salt technical melting point is 212-214 $\pm$ 1 °C. At this melting point the product (asulam- sodium salt technical) begins to decompose.

CBRS Comment Regarding Data provided for Melting point:

This deficiency is resolved for the asulam-sodium salt TGAI.

Data Requirement: Regarding Solubility (Guideline # 63-8)

Asulam Product and Residue Chemistry Reregistration Standard Update (dated 1/15/91) indicated that Rhone-Poulenc has responded to this data requirement for the 86.4% TGAI (MRID 40751501; EPA Reg. No. 264-451); however, solubility of the product in water and organic solvents must be determined at 20 or 25 °C.

Registrant's Response to Data Requirement: Regarding Solubility (Guideline # 63-8)

The registrant has provided data (MRID 42342003) on the solubility of asulam-sodium salt TGAI with 90.7% purity (batch No. EN 50005). The solubility of asulam (in n-hexane, toluene, methylene chloride, methanol, 2-propanol, n-octanol, acetone, and ethyl acetate) was determined using a HPLC/UV method at 270 nm. Asulam-sodium salt technical was dissolved in each solvent at room temperature, the solutions were equilibrated at 30°C for 24 hours and then at 25 °C for 24 hours. Then the solutions were centrifuged at 2000 r.p.m. and filtered through Chromafil 0.45 μm

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filters. Aliquots of the filtered solutions were diluted with water in a 100 ml volumetric flasks, in duplicate. For solutions in n-hexane, methylene chloride, toluene, and ethyl acetate (not miscible with water) the aliquots were evaporated to dryness under nitrogen and the residue redissolved in water and analyzed by HPLC. Under the chromatographic conditions used (pH 3 mobile phase), the asulam-sodium salt is dissociated and subsequently protonated to free asulam, so the retention time of the "salt" is the same as asulam.

Solubility of asulam-sodium salt in the solvents was estimated to be as follow:

Solvent	Temperature °C	pH	g/100 ml
water	10, 20, & 3 5	6.5	>100
water	20	5 & 9	>100
n-hexane	25	-----	0.000059
toluene	25	-----	0.00014
methylene chloride	25	-----	0.0011
ethyl acetate	25	-----	0.011
n-octanol	25	-----	0.0019
acetone	25	-----	0.090
2-propanol	25	-----	0.028
methanol	25	-----	3.30

CBRS Comments: Regarding Solubility (Guideline # 63-8)

This deficiency is resolved for the asulam-sodium salt TGAI.

Data Requirement: Regarding Dissociation Constant (Guideline # 63-10)

Asulam Product and Residue Chemistry Reregistration Standard Update (dated 1/15/91) indicated that Rhone-Poulenc has responded to data requirement for the 86.4% T (MRID 40751501; EPA Reg. No. 264-451); however, the method used and the test substance (TGAI or PAI) must be specified.

Registrant's Response to Data Requirement: Regarding dissociation Constant (Guideline # 63-10)

The registrant has provided data (MRID 42342004) on the dissociation constant of asulam-sodium salt with 90.7% purity. The dissociation constant of asulam-sodium salt was determined using a pH-meter and 0.01 M HCl. Asulam-sodium salt technical was dissolved in water (250 mg/l) and this solution (triplicate)

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was titrated with 0.01 M HCl at room temperature. The dissociation constant K_a of asulam was determined to be 7.53 X 10^{-6} (pK_a = 5.12), corresponding to a pK_b for asulam sodium of 8.88.

CBRS Comments: Regarding Dissociation Constant (Guideline # 63-10)

This deficiency is resolved for the asulam-sodium salt T.

Data Requirement: Regarding Storage Stability & Corrosion Characteristics (Guideline # 63-17 & 63-20)

Asulam Product and Residue Chemistry Reregistration Standard Update (dated 1/15/91) indicated that Rhone-Poulenc has not responded to these data requirements for the 86.4% TGAI (EPA Reg. No. 264-451); therefore, data are required to satisfy these Physical/Chemical characteristics.

Registrant's Response to Data Requirement: Regarding Storage Stability & Corrosion Characteristics (Guideline # 63-17 & 63-20)

The registrant, in correspondence dated 6/2/92 (MRID 42342000) has requested data waivers for asulam-sodium salt TGAI regarding product chemistry product-specific requirements storage stability and corrosion characteristics (63-17 and 63-20). Because, "according to 40 CFR 158.190, physical and chemical characteristics, both studies are only required for manufacturing-use products (MP). Our asulam sodium salt material is considered the technical grade active ingredient (TGAI)."

CBRS Comments: Regarding Storage Stability & Corrosion Characteristic (Guideline # 63-17 & 63-20)

CBRS presently cannot make a recommendation regarding the data waiver requests for asulam-sodium salt storage stability and corrosion characteristics (Guideline # 63-17 and 63-20), because it is not clear to us whether asulam-sodium salt is an unregistered TGAI and data are submitted to support the registration of end-use products, or it is a MP as well as a TGAI (see our note to PMs in this memo).

Note To Joanne I. Miller (RD PM 23) and Linda Propst (SRRD PM 73):

CBRS has noticed that there are some discrepancies between the Asulam Product Chemistry Chapter (8/28/87) and the Asulam Product and Residue Chemistry Reregistration Standard Update dated 1/15/91 regarding asulam (acid) 86.4% T (EPA Reg. No. 264-451; PC Code No. 106901) and that of asulam-sodium salt T (PC Code No. 106902) as follows:

1. We noticed that the Asulam Registration Standard (dated, 8/28/87) has considered product chemistry data requirements (at least 63-2 to 63-20) only for the **asulam (acid) 86.4% T (PC Code No. 106901; EPA Reg. No. 264-451)** which is the TGAI and sole constituent of the MP. Therefore, all product chemistry data (generic and specific) for asulam (acid) 86.4% T were required.

2. Subsequently, the Asulam Product and Residue Chemistry Reregistration Standard Update (1/15/91) seems to have considered the data requirements for asulam (acid) 86.4% T, EPA Reg. No. **264-451) even though the new undated CSF (received 7/18/88) and Preliminary analysis data (MRID 40751501) indicate that the active ingredient is [redacted] asulam-sodium salt (PC Code 106902) rather than asulam (acid) 86.4% T. Also, the last steps in the manufacturing processes presented in the 8/28/87 Registration Standard and the 1/15/91 Update were different (resulting in acid vs. sodium salt).**

3. According to REFS (Reference File System) the following product transfers occurred on 4/25/88 from company No. 359 (Rhone-Poulenc Inc.) to Company 264 (Rhone-Poulenc AG company): a. **asulam 86.4% technical (acid)**: [old EPA No. 359-680; **new EPA Reg. No. 264-451**]; b. Asulox an **end-use product with 36.2% asulam-sodium salt:**[old EPA No. 359-662 ; new **EPA Reg. No. 264-447.**]

4. Therefore, based on item Nos. 1, 2, and 3 above two technical active ingredients, asulam (acid) 86.4% T and asulam-sodium salt 86.4% T (with different CSF and preliminary analysis data), have both been supported by the registrant at various points in time, and somehow both have the same registration number (EPA Reg. No. 264-451). It could be that sometime between the 12/87 Guidance Document and the 1/15/91 Update, ai was changed from the acid to the sodium salt [see p. 21 where MP ingredient statements must be in terms of asulam (acid) whereas EPs must be in terms of asulam sodium salt]. We also note that Rhone-Poulenc, in its 6/2/92 submission (MRID 423420-00), referred to the test substance as a 90.7% TGAI asulam sodium salt (EPA ID. No. 264-LNL) as if they are attempting to register a new product. Personal communication with Joanne Miller (8/20/92)

revealed that 264-LNL is a 87.6% MP of asulam sodium salt.

5. The submitted data reviewed herein are all for the asulam-sodium salt TGAI (90.7%).

6. According to Joanne I. Miller [personal communication (7/20/92)], there is only one asulam (acid) 86.4% T that is registered (EPA Reg. No. 264-451). The only asulam sodium salt product that is registered is an end-use product containing 36.2% asulam sodium salt (EPA Reg. No. 264-447).

CBRS is not sure whether asulam-sodium salt is an unregistered TGAI and the registrant is submitting data using it as test substance to support the registration of an end-use product, or if it is an MP containing only the TGAI. Has the registrant changed the ai in the MP (264-451) from the acid to the sodium salt? Is an MP (264-LNL) containing asulam sodium salt a pending product? We are interested to know if the Registrant wants to support and register MPs containing both active ingredients (asulam acid and asulam sodium salt), or only one of them.

Regardless of whether asulam acid and/or sodium salt serve as active ingredients in end-use products, the following general rules apply: (i) an MP (i.e., a registered product for formulation purposes, whether the TGAI is the sole component or if there are intentionally-added inerts) requires product specific data (i.e., the MP serves as test substance); (ii) every different ai (Chemical No.) in an EP requires at least generic data (i.e., using TGAI as test substance) to support MP and EP registration (even if a TGAI is not isolated or is not the sole component of an MP) and (iii) if the TGAI is the sole component of an MP then, in effect, all generic and product specific data are required. Once CBRS knows the registrant's intentions (see items 1 to 6, above), we can render final decisions.

cc: Asulam-sodium salt S.F., R.F., Reg. Sted. File, List A file, L. Propst (PM 73/SRRD), J. Miller (PM 23/RD), F. Chow, F. Toghrol, Circ.,

RDI: W. Hazel (8/24/92): M. Metzger (8/25/92): E Zager (8/26/92
H7509C:CBII:RS:F.Toghrol:F.T.:RM:804B:CM#2:(703)305-7887:7/16/92.

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PRODUCT CHEMISTRY

Case No.: 0265 Case Name Asulam-sodium salt
Chemical No(s).: 106902
Chemical Name(s): Methyl sulfanilylcarbamate
Registrant: Rhone-Poulenc

Guideline Number	Is requirement applicable?	Does summary or available information indicate MRID is a candidate for Phase 5 review?	Are additional data required[a]?	MRID Number[b]
61-1	Y	N	Y[1]	40751501
61-2(a)	Y	Y	N	40751501
61-2(b)	Y	N	Y[2]	40751501
62-1	Y	Y	N	40751501
62-2	Y	N	Y[3]	40751501
62-3	Y	N	Y[4]	40751501
63-2	Y	Y	N	40751501
63-3	Y	Y	N	40751501
63-4	Y	Y	N	42342001
63-5	Y	Y	N	42342002
63-6	N	N/A	N	
63-7	Y	Y	N	40751501
63-8	Y	Y	N	42342003
63-9	Y	Y	N	40751501
63-10	Y	Y	N	42342004
63-11	Y	Y	N	401751501
63-12	Y	Y	N	40751501
63-13	Y	N	Y[5]	40751501
63-14	N	N/A	N[6]	
63-15	N	N/A	N[6]	
63-16	N	N/A	N[6]	
63-17	Y	N	Y[7]	
63-18	N	N/A	N[6]	
63-19	N	N/A	N[6]	
63-20	Y	N	Y[7]	

Key: Y=yes; N=no; I=a decision cannot be made at this time; S=fully satisfies requirement; P=partially; N/A=not applicable; U=unsatisfactory.

[a]A superscript in this column indicates any necessary footnotes, including responses to new data waiver/time extension requests.

[b]MRID No. is not listed if study or summary are found to be inadequate.

Note: <u>All</u> data requirements must be reassessed once a response is recieved to the subject memo (F. Toghrol, CBRS No. 10086, DP Barcode D179485) because there are questions about what has served as test substance in the past, what chemical (acid or Na salt) serves as ai, and whether one or both ai's are contained within MPs and EPs.

1. Phone-Poulenc has responded to data requirements for the 86.4% T; however, not all impurities present at ≥ 0.1% were identified. For remaining impurities, the following information must be provided: the chemical name and nominal concentration of each impurity of toxicological significance associated with the active ingredient or present in any sample at a level equal to or greater than 0.1% by weight of the TGAI.

2. Phone-Poulenc has responded to data requirements for the 86.4% T; however, not all impurities present at ≥ 0.1% in the TGAI have been identified; upon identification, a discussion regarding the origin of any of these impurities present at ≥ 0.1% will be required. In addition, discussion of the following is required: the possible degradation of ingredients after production, and possible contamination from packaging materials or production equipment.

3. Rhone-Poulenc has responded to data requirements for the 86.4% T; however, not all impurities present at ≥ 0.1% in the TGAI have been identified; upon identification, upper certified limits will be required for any of these impurities of toxicological significance.

4. Rhone-Poulenc has responded to data requirements for the 86.4% T; however, not all impurities present at ≥ 0.1% in the TGAI have been identified; upon identification, analytical methods will be required for any of these impurities of toxicological significance.

5. Rhone-Poulenc has responded to data requirements for the 85.4% T; however, data pertaining to the stability of the product in the presence of sunlight, metals, and metal ions are required.

6. According to Asulam Reregistration Standard (dated, 1/15/91) these data are not required.

7. These data are required, the registrant must clarify whether submitted data for asulam-sodium salt T are submitted to support the registration of the end-use product, or whether the registrant wants to register both TGAIs (asulam acid 86.4% T and asulam-sodium salt).